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Editorial

Reactive Oxygen Species and Red Ox State During *In Vitro* Fertilization

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Editorial

The role of Reactive Oxygen Species (ROS) and redox state in reproductive processes is still controversial. The presence of antioxidant enzymes in several mammalian species suggests that defense mechanisms are conserved and would be important for the last stages of oocyte maturation and for early embryo development [1]. However, in some species, as in the bovine, the addition of antioxidants to the culture medium resulted in a decrease in the percentage of blastocysts produced *in vitro* [2]. Moreover, in sperm, ROS have been described to have an important participation in the regulation of all the functional parameters, including motility, capacitation, sperm-zona pellucida interaction, acrosome reaction and sperm-oocyte fusion [3,4].

Several studies propose that physiological ranges of ROS concentration in the follicular fluid may be the result of the balance between pro-oxidant systems and scavengers and would be necessary for normal oocyte development [1]. Therefore, certain ROS levels could be indicators of healthy oocytes, while their excess would indicate oxidative stress, which could compromise *In* Vitro Fertilization (IVF) [5-8]. The total antioxidant capacity of the follicular fluid is considered a predictive marker for a successful IVF [7]. The beneficial effect of the follicular fluid against oxidative damage would be due in part to a high Superoxide Dismutase (SOD) activity, which has been shown to have a positive correlation with an increase in cytoplasm maturation in the porcine oocyte [9]. In contrast, in humans, a high SOD activity has been associated with oocytes which failed to be fertilized [10], but physiological concentrations of another antioxidant enzyme, glutathione peroxidase, presented a positive correlation with IVF rates [11].

In addition, the antioxidant deposits (as mRNA or proteins) in the oocyte during its growth and maturation would also be important for embryos to obtain developmental competence [1]. In somatic cells, the presence of a mechanism of regulation of the synthesis of antioxidants in pre and post translation stages has been proved [12-14]. This could be relevant for oocytes during the maturation process, in which translation and post-translation regulation of protein synthesis prevail [15-17]. In the mouse, mRNA which codify for glutathione peroxidase, SOD and γ-glutamylcysteine synthetase (important enzyme for glutathione synthesis) both in immature and mature oocytes was detected, while in humans the regulation of glutathione peroxidase and SOD transcripts has been documented [18]. As regards catalase, mRNA has been found in fertilized oocytes in the mouse and bovine [19], but not in humans [18]. Catalase activity has also been detected in immature and *in vitro* matured bovine oocytes [20].

It has been shown that several transcription factors involved in developmental processes are regulated by the intracellular red ox potential [21-26]. These factors are sensitive to oxidation or S-glutathionylation by ROS and require NAD (P) H o NAD $(P)^+$ [27]. In somatic cells, it has been observed that red ox state and ROS levels are negatively related. A high intracellular oxidative activity (for example, due to the increase in the mitochondrial oxygen consumption rate) is usually associated with a decrease in ROS production [28]. In the mouse, it has been demonstrated that redox state and ROS production regulation have a fundamental importance in early embryo development [27].

In the bovine, we found clear and distinctive metabolic patterns as regards redox activity and fluctuations in ROS production between non-activated oocytes, *in vitro* fertilized and parthenogenetically activated oocytes; sperm-activated oocytes presented an increase in oxidative activity corresponding with the initiation of pronuclear formation and first mitotic division, suggesting increased demands of energy for these events [29]. This increase can be related with results obtained by other groups who described that one and two cell bovine embryos are dependent on mitochondrial oxidative phosphorylation for energy supply, consuming oxidative substrates to produce ATP [30,31]. Coincidently, a higher oxygen consumption rate was detected prior to cleavage in bovine zygotes [32]. It remains to be studied if these metabolic patterns are shared by other species, including humans.

In conclusion, there is still much to investigate about the participation of ROS and the influence of red ox state in oocyte maturation, IVF and embryo development. The study of the characteristic behaviors in red ox activity and ROS level fluctuations during early development could be integrated in our understanding of indicators of oocyte quality and embryo developmental competence. Therefore, future works should be carried out to clarify the role of these metabolic parameters in order to improve IVF and other assisted reproduction techniques.

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